Appendix 12c

REVIEW
to occupy the academic position:

''Professor''	
''Associate Professor''	X
	one of the academic positions indicated shall be marked with the sign "X"

Candidates to occupy the position:

1	Chief assit	PhD	Tsvetelina	Georgieva	Angelova	UCTM
№	academic position	scientific degree	name	middle name	last name	workplace

Scientific area:

5	Technical sciences
code	name

Professional area:

5.11	Biotechnology
code	name

Scientific specialty:

Technology of biologically active substances

The competition has been announced:

96	17.11.2023	Biotechnology	Faculty of Chemical and Systems Engineering
in SG issue	date	for the needs of the Department	Faculty

The review was written by:

professor	PhD	Yana	Dimitrova	Chekalarova	UCTM
academic position	scientific degree	name	middle name	last name	workplace

1. Review for the candidate:

Chief assist	PhD	Tsvetelina	Georgieva	Angelova
academic position	scientific degree	name	middle name	last name

1.1. Completion of the provided documents:

A) The competition documents are in full compliance with the Regulations	3 points	**x**

B) The documents are complete but do not fully comply with the requirements of the Regulations	2 points	
C) The documents are not completed in accordance with the requirements of the Regulations	0 points	
		one of the answers given is marked with the sign "X"

Missing documents and violated requirements must be described if response C is marked.
All the necessary documents for this competition have been submitted and fully comply with the Rules of the UCTM. Accordingly, the candidate participated in the competition with 37 publications, of which 29 publications are in publications that are referenced and indexed in world databases (P4+P7) and 8 publications are in publications that are published in non-refereed journals with scientific review (P8). A study guide for students was also presented for the competition.

1.2. Meeting the minimum requirements under the Regulations:

A) The candidate meets the minimum requirements	20 points	X
B) The candidate doesn't meet the minimum requirements	0 points	
		one of the answers given is marked with the sign "X"

It must be filled in if answer B is marked. The publication activity of the candidate is analyzed. The response of the results achieved (quoted) is analyzed.
The candidate meets the minimum requirements according to the Rules of the UCTM. It should be noted that most of the indicators for which documents were submitted exceeded the requirements for the competition according to indicators as follows: indicator 1 - 50/**50**; 3 or 4 - 100/**100.4**; D – 200/**213.7**; D – 50/**190**; E – 0/**90**. Indicator 1: dissertation – 50 points. Indicator 4 /10 articles/ out of 100 points - 100.4 points. Indicator 12: out of 50 items - 10 citations in world databases - 100 items + 1 review in scientific publications - 10 items = 110 items. Indicator 23: Published university textbook - 10 points - no competition points are required for this indicator, but material is presented. According to indicator 4, a habilitation thesis is presented, which is based on 10 publications in refereed publications, with which the candidate has not participated in previous procedures. Ten of these publications are referenced and indexed in SCOPUS, and three of them are also referenced in Web Sci (2,7,8).

1.3. Relevance of scientific and / or applied research:

A) The research is relevant. Part of the research is pioneering (no results are known on the topic by other authors)	7 points	
B) Research is relevant. Results from other authors are known for each of the topics and / or applications studied.	5 points	X

C) Most of the research is relevant, but also some results are presented that have no scientific and / or applied value	3 points	
D) The smaller part of the research is relevant	2 points	
E) Research is not relevant	0 points	
		one of the answers given is marked with the sign "X"

The evaluation of the relevance of the research must be substantiated.
The results of the studies, which were conducted by the Assist. Prof. Tsvetelina Foteva and, accordingly, the materials included in the competition are relevant and summarized in the following main areas: 1. Antimicrobial activity of polymeric materials containing metal ions. 2. Biocompatibility and cytotoxicity of hybrid materials. 3. Synthesis, characterization, analysis, and activity research of biomolecules with the aim of their application in medicine, pharmacy, and diagnostics. These studies are mainly of applied importance in the development of new inorganic-organic hybrid materials with potential application in the field of biomedicine, in which the integrated metal nanoparticles contribute to improving their properties in terms of prolonged release time or activity of the active substance, making them attractive for application as drug carriers, in imaging, in tissue regeneration, in artificial implants, and so on. The small size and irregular shape of the nanoparticles is also a prerequisite for the improved antibacterial and antifungal activity of the hybrids. The developed hybrid materials have been evaluated for their biocompatibility, cytotoxicity, proallergic and anticarcinogenic effects, making them suitable for use in ceramic nanocoatings, bone implants, plastic surgery, etc. In the context of one of the novel directions in the development of therapeutic approaches in oncology - targeted therapy, the deputy head. Foteva and her team have been involved in developments related to the design, synthesis and study of antimicrobial peptides with potential anti-tumour activity, and a liquid chromatography method with UV detection has been introduced into Direction 3 of the scientific topics developed by the candidate in the competition, with important applied importance for the detection of banned active substances in food supplements and those used in sport.

1.4. Knowledge of the problems subject of research:

A) The candidate knows in detail the achievements of other authors on the researched topics and/or applications	6 points	X
B) The candidate is partially familiar with the achieved results on the researched topics and / or applications	4 points	
C) The candidate has no prior knowledge of the status of the researched problems	0 points	
		one of the answers given is marked with the sign "X"

The evaluation must be substantiated if answer C is marked.
I believe that Assist. Prof. Foteva is an expert in the field in which she carries out her scientific work, which is confirmed by the well-structured contributions in three main areas, based on the publications submitted for the competition, some of which she is the first author of. The scientific interests of Foteva's views on the application of new inorganic materials are also confirmed by a published review article focusing on the use of nanotechnology in cosmetics and, more specifically, the methodological approaches used to overcome the biological barriers of materials and their safety.

1.5. Type of research:

A) Theoretical	4 points	
B) Applied	4 points	X
C) Theoretical with application elements	4 points	
D) It does not correspond to the level specified in the Act for the Development of the Academic Staff in the Republic of Bulgaria and the Regulations	0 points	
		one of the answers given is marked with the sign "X"

The level of research must be substantiated if answer D is marked.
The research of the Assist. Prof. Tsvetelina Foteva is exclusively scientific and applied and can be summarised in several main directions: 1. Development and characterisation of new hybrid polymer materials with metal nanoparticles for application in various fields of biomedicine, including artificial implants, drug carriers, materials used in imaging, tissue regeneration.To be considered as viable biomaterials, the materials developed by Assistant Professor Foteva and her team must have antibacterial and antifungal activity, be biocompatible, have low toxicity and side effects, be able to penetrate biological barriers (nanoparticle materials) and have potential anti-tumour activity (targeted therapy applications). 2. Introduction of methods for the detection of harmful substances in widely used food supplements or in sports. 3. Design, synthesis and characterisation of biomolecules with potential application in medicine, in particular in oncology, including 1) the antimicrobial peptide with additional antitumour activity by introducing unnatural amino acids into its structure; 2) novel bioconjugates of monofluorinated analogues of BIM-23052 with a second pharmacophore naphthalimide, caffeic acid or the tripeptide Arg-Gly-Asp. 4. The synthesis and characterisation of composite materials has been carried out with a view to their potential application as adjuvants in cancer therapy. It was found that the cytotoxicity of the developed hybrid materials containing SiO2/cellulose and copper from different sources was closely related to critical factors that should be considered in the future when developing such materials, such as the source of sulphate or nitrate, the amount of copper ions in the composite materials, the cell type and the incubation time.

1.6. Objectives of the research:

A) Realistic and of scientific and / or applied interest	8 points	X
B) Realistic, but not of scientific and / or applied interest	4 points	
C) Unattainable (unrealistic)	0 points	
		one of the answers given is marked with the sign "X"

Objectives must be specified. The type of the set objectives must be justified.
1. The presented objectives have rather an applied contribution related to the synthesis, characterisation and study of antimicrobial and antifungal protective effect of different in nature new type of hybrid materials, with included silver nanoparticles, copper or zinc, lignocellulosic waste with silver coating, or loaded with nanoparticle material to find application in diverse areas of human activity, including food industry, pharmacy, medicine, agriculture, wastewater treatment. 2. Hybrid materials of different nature have been investigated for biocompatibility, cytotoxicity and anti-tumour activity, making them potentially applicable in tissue engineering, dentistry, catheter fabrication. 3. Synthesis and characterisation of cytotoxicity, antiproliferative and antimicrobial activity of target molecules, bioconjugates of peptides containing as pharmacophore 1,8-naphthalimide glycine, caffeic acid or the unnatural amino acid. 4. Investigation of the antimicrobial activity of specially designed derivatives of memantine.

1.7. Methods of research:

A) Adequate to research and set scientific objectives and /or applications	8 points	X
B) Partially appropriate, enabling part of the scientific objectives and / or applications to be achieved	4 points	
C) Inappropriate methods	0 points	
		one of the answers given is marked with the sign "X"

Methods must be specified. The type of methods used is justified.
The methods used are appropriate and fully in line with the objectives and planned tasks of the research. Assist. Prof. Foteva used a combination of innovative and original approaches to develop new hybrid biomaterials with potential applications in biomedicine and other areas of human activity. The methods used can be summarised as follows: 1. Methods for the design and synthesis of new hybrid materials based on carboxymethyl cellulose (CMC) and TEOS with incorporated silver nanoparticles by the sol-gel method. 2. Characterisation of the hybrid materials by infrared spectroscopy with Fourier transform (FTIR), differential thermogravimetry (DTG) and thermogravimetric analysis (TG), UV-Vis spectroscopy and transmission electron microscopy, photocatalytic tests.

3. Methods of antibacterial activity against gram-positive (Bacillus subtilis NBIMCC 3562), gram-negative (Escherichia coli NBIMCC K12 407) bacteria and yeasts Candida albicans NBIMCC 74, Saccharomyces cerevisiae 537 using two methods - the inhibition zones formed around materials and reduction of cell growth.
4. Methods of antifungal activity against the opportunistic pathogenic fungi Candida albicans 74.
5. Characterisation of the biomaterials in vitro by cell culture: evaluation of cytotoxicity, morphological characterisation, cell survival, fluorescence observation of nuclei and actin filaments of fibroblasts on cell line L929, cytotoxicity against lung cancer cells, cell line (A549) and primary human umbilical cord endothelial cells. The anticancer potential was tested against a panel of tumour cell lines including the human mammary carcinoma cell lines MCF-7 (ER+, PR+ and Her-2-); MDA-MB-231 (ER-, PR- and Her-2-) and the BALB 3T3 (mouse embryonic fibroblasts) and MCF-10A (human mammary epithelial cells) cell lines. IC50 values and selectivity index (SI) were calculated.
6. An HPLC/DAD method has been developed for the simultaneous determination of 13 substances with a steroid structure in sports nutrition supplements: testosterone, testosterone propionate, testosterone enanthate, methyltestosterone, nandrolone, nandrolone propionate, nandrolone decanoate, methandienone, androstenedione, trenbolone, trenbolone acetate, trenbolone enanthate and boldenone undecylenate.

1.8. Candidate research contributions:

A) With lasting scientific and / or applied response, they form the basis for new research and applications	20 points	X
B) They are of significant scientific and / or applied interest, complete and / or summarize previous research	16 points	
C) They are of scientific and / or applied interest	12 points	
D) Lack of significant contributions	8 points	
E) Lack of contributions	0 points	
		one of the answers given is marked with the sign "X"

Contributions must be specified. The type of results achieved must be justified.
The contributions are grouped into three main thematic areas, based on the publications with which the deputy chief executive has participated. Foteva participates in the competition, which are very well formulated. 1) I consider as significant scientific and applied contributions the development and characterisation of three types of inorganic-organic hybrid materials based on silica, hydroxypropylcellulose (HPC), hydroxypropylmethylcellulose (HPMC), carboxymethylcellulose (CMC) and with incorporated silver nanoparticles (AgNPs) obtained by the sol-gel method.The morphology was studied by UV-Vis, TEM, DTA/TG analysis and materials containing zinc nanoparticles. Their antibacterial and antifungal properties were determined against the reference strains B. subtilis NBIMCC 3562 and E. coli K12, Candida albicans 74 and clinical strains Salmonella and Shigella, Klebsiella. The antimicrobial

activity of the materials was tested against the moulds Asp. niger 371 and P. chrysogenum 2303, where a good antifungal effect was demonstrated.

The third class of synthesised hybrid materials containing SiO_2, HPC and copper ions were, after characterisation by XRD, IR and UV-Vis analyses, evaluated for their antimicrobial potential against gram-positive bacteria (Bacillus subtilis NBIMCC 3562), gram-negative bacteria (Escherichia coli K12 NBIMCC 407) and yeast (Candida albicans NBIMCC 74).

Nanocomposite materials containing SiO_2, ZnO, TiO_2 and reduced graphene oxide (RGO), as well as materials based on TiO_2 and SeO_2, were also investigated. All of them show good antibacterial properties, making them suitable and applicable in a number of biomedical fields.Research has been carried out on the possibility of preserving wood by modifying it with alkali-activated hydrolyzed lignin, Cu_2S and maleic anhydride by the infiltration method, and the influence of the process on some operational properties of the wood material has been investigated. All modified samples exhibited antibacterial resistance to Gram-negative bacteria.

2) The cell survival and adhesion of 3T3 mouse fibroblasts on the hybrid materials with silver nanoparticles was investigated. The results obtained showed increased cell proliferation of 3T3 cells, more pronounced after 48 hours of culture. The higher the silver content, the lower the cell survival. This can be explained by the properties of silver as an antimicrobial agent and by the higher roughness and contact angle determined during the structural characterisation of silver-containing materials.A bactericidal effect was found for all three hybrid materials used with silver nanoparticles, with concentration-dependent activity observed.

The biocompatibility and antifungal properties of hybrid materials containing SiO_2/pectin and silver were investigated. The MTT assay showed good mouse fibroblast survival and satisfactory cytoskeletal organisation in materials containing up to 1 wt% silver. At the same time, the composites showed antifungal activity against the growth of C. albicans 74, making them a potential candidate material for in vivo implants.

An interesting direction in the studies of the principal assistant. Foteva also represents the study of the cytotoxicity of hybrid materials containing SiO_2/cellulose and copper from different sources. The results show that the cytotoxic effect of the materials used depends on the Cu source used (sulphate or nitrate), the amount of copper ions in the composite materials, the cell type and the incubation time. Cell viability was affected by both types of composites, with the material obtained with $CuSO_4.5H_2O$ being more cytotoxic.Two cancer cell lines (lung cells (A549) and endothelial cells (HUVEC)) were investigated, with A549 cells showing greater sensitivity. The synthesised composites can thus be used for further research and development with the aim of applying them as a new and/or adjuvant cancer therapy.

3) New bioconjugates of monofluorinated analogs of BIM-23052 containing a second pharmacophore naphthalimide, caffeic acid or the tripeptide Arg-Gly-Asp were evaluated. The anticancer potential was evaluated against a panel of tumour cell lines including the human mammary carcinoma cell lines MCF-7 (ER+, PR+ and Her-2); MDA-MB-231 (ER-, PR- and Her-2-) and the BALB 3T3 (mouse embryonic fibroblasts) and MCF-10A (human mammary epithelial cells) cell lines. The most active compound was a bioconjugate containing naphthalimide as the second active component in the molecule.Single- and double-sequence analogs of the antimicrobial peptide $(KLAKLAK)_2$-NH_2 with additional antitumour activity were designed, synthesized and characterised by introducing the unnatural amino acids Nle and β-Ala into its primary structure. Antibacterial properties, antiproliferative effect, cytotoxicity of all newly synthesized analogues and conjugates of

(KLAKLAK)2-NH2 were investigated and important structure-biological activity relationships were deduced.

1.9. Participation of the candidate in the achievement of the presented results:

A) The candidate has at least an equal participation in the submitted papers	8 points	
B) The candidate has at least an equal participation in most of the submitted papers	7 points	X
C) The candidate has a secondary participation in most of the submitted papers	4 points	
D) The candidate participation is unnoticeable	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the items C or D is marked.
There are no separation protocols in the documents, so I assume that the candidate is equally involved in the works presented. Assist. Prof. Foteva is the first author of about 35% of all the publications submitted to the competition (13 articles out of a total of 37 in the list of publications) and 32% as the second or last author /12 articles out of a total of 37/.

1.10. Pedagogical activity:

A) The candidate has effective and sufficient pedagogical activity at the university. The textbooks issued are modern and useful (they meet the requirements of the Regulations). The work with undergraduate and doctoral students is at a high professional level.	8 points	X
B) The candidate has sufficient pedagogical activity at the university. The textbooks issued satisfy the requirements of the Regulations.	6 points	
C) The pedagogical activity and / or textbooks issued are insufficient (do not meet the requirements of the Regulations)	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the items B or C is marked.
Assist. Prof. Tsvetelina Foteva has been actively teaching at UCTM-Sofia for a period of 7 years after joining the Department of Biotechnology as an assistant. In the last three years of her career, she has taught 3 lecture courses for Bachelor of Chemical Engineering with German language teaching for 2nd, 3rd and 4th year full-time students, 3 lecture courses for Biotechnology for 3rd and 4th year full-time and distance learners respectively, and a lecture course on Industrial Biotechnologies in English for ERASMUS students. An excellent impression is made by the huge number of graduates who successfully defended under her guidance or as a consultant. For the period from 2017 to 2023, she supervised a total of eleven bachelor's degree graduates and three master's degree graduates. As a scientific

consultant during the period from 2013 to 2016, under her guidance, successfully defended diploma thesis for the n.st. bachelor four students and for master three students as four of the diploma theses were developed in the city of Hamburg, Germany and one of them is in English. Ch. assistant Foteva is the co-author of a textbook "Electronic form of a practical course in Microbiology", UCTM-Sofia, published in 2015, which is intended for students of Biotechnology and Biomedical Engineering at UCTM-Sofia, being tailored to the specific requirements of the study programs of these specialties.

1.11. Critical notes:

A) Lack of critical notes	8 points	
B) Critical notes of a technical nature	7 points	X
C) Critical notes that would partially improve the results achieved in a small part of the research	5 points	
D) Critical notes that would partially improve the results achieved in most of the research	3 points	
E) Significant critical notes	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the answers C, D or E is marked.
On the basis of the publications presented in the competition, the contributions are grouped into three main directions, which I consider to be excellently formulated and systematised. In my opinion, two of the candidate's developments do not belong to any of the three directions and should be presented independently, namely her review article on the analysis of the role and application of nanotechnology in the cosmetic industry, which is included in the first direction "Antimicrobial activity of polymeric materials containing metal ions" and the validations HPLC method with UV detection for the determination of banned substances in biological samples, included in the third line "Synthesis, characterisation, analysis and activity research of biomolecules for their application in medicine, pharmacy and diagnostics". I would recommend adding to the general list of publications a reference to its indexing in major databases such as Scopus and WoS and its WoS quartile.

1.12. Conclusion

A) The evaluation of the candidate’s activity is **POSITIVE**	This evaluation is assigned to a total number of at least 65 points	X
B) The evaluation of the candidate’s activity is **NEGATIVE**	This evaluation is assigned to a total number below 65 points	
		one of the answers given is marked with the sign "X"

To be filled in if requested by the reviewer

Based on the analysis of the scientific indicators, the relevance and significance of the results of her publications and contributions presented in the summary, as well as an assessment of the research and teaching activities of the candidate, my assessment is POSITIVE /96 points/. This gives me reason to confidently propose to the members of the distinguished Scientific Jury to vote in favour of awarding the academic position of "DOCENT" at UCTM-Sofia to the Assist. Prof. Tsvetelina FOTEVA according to the announced competition (GP No. 96 of 17.11.2023) in the professional direction 5.11. "Biotechnologies", in the scientific speciality "Technology of biologically active substances".

14.02.2024	The review was written by:	
date		signature